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10/554,409	04/23/2008	Hans Gronlund	1768-139	4548

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EXAMINER	
ROONEY, NORA MAUREEN	

ART UNIT	PAPER NUMBER
1644	

NOTIFICATION DATE	DELIVERY MODE
06/21/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTO-PAT-Email@rfem.com

Office Action Summary	Application No.	Applicant(s)	
	10/554,409	GRONLUND ET AL.	
	Examiner	Art Unit	
	NORA M. ROONEY	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 April 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-41* is/are pending in the application.

4a) Of the above claim(s) *34-36 and 39-41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-33,37 and 38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 October 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *03/22/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 22-41 are pending.

2. Applicant's election with traverse of Group I, claims 22-33 and 37-38 in the reply filed on 04/16/2010 is acknowledged. The traversal is on the ground(s) that:

Applicant has submitted a 37 CFR 1.131 Declaration of Hans Gronlund and evidence in Exhibits A1 and A2 on 05/04/2010 to antedate the Vailes et al. reference.

Additionally, Applicant argues:

> For the record, Applicants also take issue with the examiner's assertion that the teachings of the George reference when combined with the teachings of the Vailes reference, are sufficient to render the present invention obvious, such that the claims of this application lack a special technical feature over the teachings of the references. Vailes et al. were seeking to engineer a recombinant Fel d 1 with antibody binding "comparable to that of the natural allergen." They further noted (second paragraph, second column of first page of the article) that "production of recombinant (r) Fel d 1 has been challenging .... " Vailes et al. then report on the preparation of a recombinant Fel d 1 having a 19 amino acid linker. One of skill in the art reading Vailes would come away with the clear understanding that a recombinant Fel d 1 is a challenging fusion product to prepare and that a lengthy linker is required to mimic the natural protein.
>
> Turning to the George reference, Applicants respectfully submit that the examiner misinterpreted Tables II - VII. These tables are not teaching the skilled person to use amino acid pairs as the linker; rather they are investigating the propensity of amino acid pairs within longer linkers. Page 875, first column, first sentence under the heading "Dipeptide propensities for linkers," explains that the authors are considering "dipeptide propensities for all linkers and medium sized linkers." The headings in Tables III and IV make it clear that the authors are considering "all linkers" and "medium sized linkers," respectively - not dipeptides. Tables V and VI relate to "non-helical" and "helical" linkers, again suggesting longer linkers.
>
> George et al. then provide a rather general conclusion in the final two columns. The reference certainly does not teach the use of shorter linkers. If anything, one of skill in the art would be taught that he should seek to investigate the structure of the 19 amino acid linker in Vailes et al. with a view to introducing more tailored diads. It also is important to note that George et al. are not concerned with specific problems concerning mimicking of the properties of naturally occurring Fel d I. George et al. therefore provide no more than suggestions for a lengthy research project into the nature of the linker in Vailes et al. The authors provide only suggestions for a lengthy research project into the nature of the linker used by Vailes et al. They certainly do not give one of skill in the art any expectation that one could reduce sensitization in a patient while simultaneously maintaining the immunological properties of the protein by providing a bond or a 1-9 amino acid linker.

This is not found persuasive because 37 CFR 1.131 affidavits or declarations are appropriate to antedate a reference or activity that qualifies as prior art under 35 U.S.C. 102(a) and not under 35 U.S.C. 102(b). 37 CFR 1.131 affidavits or declarations inappropriate where the reference publication date is more than 1 year prior to applicant's or patent owner's effective filing date. The one year grace period runs from the earliest US priority date, which is the filing date of PCT/IB04/01583 on 04/22/2004. Accordingly, the 37 CFR 1.131 Declaration of Hans Gronlund and evidence submitted on 05/04/2010 is ineffective to overcome the art.

Applicant's assertion that George et al. doesn't teach the use of shorter linkers is incorrect. Applicant's attention is drawn throughout the document and specifically to page 871 where the reference teaches that:

> "The amino acids Thr, Ser, Pro and Asp were found to be desirable linker constituents. The author concluded that the preferred linker amino acids are mostly hydrophilic, often polar and usually small. The majority, 59%, of the linker residues were in coil or bend structures with a mean length of 6.5 residues, but an average flexibility when compared to other protein regions. It was suggested that pentapeptides consisting of Gly, Ser and Thr would make the best linkers for gene fusion as they residues were most strongly preferred within natural linkers."

Further, Applicant's attention is drawn to page 872, left column, last paragraph where the terms 'small linker,' 'medium linker,' and large linker' are defined as being less than 6 amino acids, 6-14 amino acids and 14 or more amino acids, respectively. The reference also teaches in

the abstract that choosing linkers is very important for obtaining desired function in chimeric multi-functional proteins. So, the teaching in George et al. is concerned with maintaining function of the individual components of the chimeric fusion protein and this teaching can be applied to the art of Vailes et al. to arrive at a Fel d 1/Fel d 2 fusion protein with a 1 to 9 amino acid linker.

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 34-36 and 39-41 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Groups, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 04/16/2010.

4. Claims 22-33 and 37-38 are currently under consideration as they read on a recombinant Fel d 1 fusion product comprising a Fel d 1 chain 1, a Fel d 1 chain 2 and a linker selected from a carbon-nitrogen bond or a peptide linker consisting of 1 to 9 amino acid residues which links the N- terminal amino acid of one chain to the C-terminal amino acid of the other chain, pharmaceutical compositions and kits thereof.

5. Applicant's IDS document filed on 03/22/2007 is acknowledged.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode

contemplated by the inventor of carrying out his invention.

7. Claims 22-33 and 37-38 *are* rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for: the fusion proteins of SEQ ID NO:4 and SEQ ID NO:35, pharmaceutical compositions and a kit thereof, does not provide reasonable enablement for: **a recombinant Fel d 1 fusion product comprising a Fel d 1 chain 1, a Fel d 1 chain 2** and a linker selected from a carbon-nitrogen bond or a peptide linker consisting of 1 to 9 amino acid residues which links the N- terminal amino acid of one chain to the C-terminal amino acid of the other chain of claim 22; wherein the linker links the N-terminal amino acid of the chain 1 to the C-terminal amino acid of the chain 2 of claim 23; wherein **the chain 1 and the chain 2** are covalently bonded together by one or more disulfide bridges into an antiparallel arrangement of claim 28; wherein **the Fel d 1 chain 1 comprises a sequence of SEQ ID NO 1, or a homologue or fragment thereof** which provides substantially the same allergenic properties as SEQ ID NO 1 of claim 29; wherein **the Fel d 1 chain 2 comprises a sequence of SEQ ID NO 2, SEQ ID NO 3, or a homologue or fragment thereof** which provides substantially the same allergenic properties as SEQ ID NO 2 or SEQ ID NO 3 of claim 30; wherein **the homologue has greater than 90% homology, preferably greater than 95% homology and particularly preferably greater than 99% homology** of claim 31; comprising **a sequence of SEQ ID NO 4** of claim 32; a homodimer consisting of two non-covalently associated **fusion products** as claimed in claim 22 of claim 33; a **pharmaceutical composition** comprising an immunotherapeutically effective amount of **the fusion product** as claimed in claim 22 and/or the homodimer as claimed in claim 33 and a pharmaceutically acceptable carrier, excipient or diluent of claim 37; and a **kit for the diagnosis of cat allergy comprising the fusion product** as claimed in claim 22 and/or the

homodimer as claimed in claim 33 and instructions for use of the kit of claim 38 and as applied to claims 24-27. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with this claim.

The specification disclosure does not enable one skilled in the art to practice the invention without an undue amount of experimentation.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention.

The specification discloses the generation of the fusion protein of SEQ ID NO:4, a pharmaceutical composition and a kit thereof.

The specification has not adequately disclosed a fusion protein comprising "a Fel d 1 chain 1," "a Fel d 1 chain 2," a homologue thereof, a homologue with greater than 99%, 95% or 90% homology, a fragment thereof, or a fusion comprising "a" sequence of SEQ ID NO:4 for the disclosed diagnostic and therapeutic purposes. The specification has not adequately disclosed

any Fel d 1 chain 1 and 2 fusion for use in the claimed invention other than the fusion proteins of SEQ ID NO:4 and SEQ ID NO:35. Without guidance in the specification as to what areas to avoid when making substitutions, deletions and additions and/or guidance regarding how to make substitutions, deletions and additions in designated areas, the resulting fusions will have unpredictable activities and binding properties. The recitation of a "fragment" reads on any two or more amino acid fragment of chains 1 and 2 of Fel d 1. The reciation of a "homologue" reads on polypeptides and peptides that are homologous over subsequences of chains 1 and 2. The term "homology" is not equivalent to the term "sequence identity." It would require undue experimentation by one of ordinary skill in the art to make and use genus of fusions encompassed because the specification offers inadequate guidance on what qualifies as a Fed d 1 chain 1 or chain 2, a homologue thereof or a fragment thereof.

The art of Blumenthal et al. teaches that a determination of IgE antibody binding to proteins cannot be made a priori based upon antigen structure (PTO-892, Reference U, whole document and page 39 of third full paragraph). Further, mutating certain amino acids may abolish antibody binding altogether as in the case of Colman et al. (PTO-892, Reference V, whole document) and Abaza et al. (PTO-892, Reference W, whole document), or could increase antibody binding as in the case of Maleki et al. (PTO-892; Reference X, whole document) which teaches that the denaturation of allergenic proteins (often the result of alteration of disulfide bridges) can increase IgE binding. In either case, the resulting genus of fusions are likely to not be useful in the claimed invention directed to fusions which have therapeutic and diagnostic purpose.

The recitation of "that retains substantially the same allergenic properties as" in claims 29 and 30 does not provide any limiting testable function such that one of ordinary skill in the art would be able to screen for fusion proteins that have the function. IgE binding, if that is meant by the recitation of allergenic properties, is not a sufficient testable function, nor is the ability to bind IgE any indication that the fusion will be able to be used diagnostically or therapeutically as disclosed in the specification.

The recitation of "a" sequence of SEQ ID NO:4 reads on any two or more amino acid subsequence of SEQ ID NO:4. It is suggested that Applicant amend the claim to recite "the sequence of SEQ ID NO:4.

Also at issue is whether or not the genus of fusions disclosed will have pharmaceutical use. In view of the absence of a specific and detailed description in Applicant's specification of how to effectively use the fusions in a pharmaceutical composition as claimed, absence of working examples providing evidence which is reasonably predictive that the claimed composition is effective for in vivo use to treat allergy, and the lack of predictability in the art at the time the invention was made, an undue amount of experimentation would be required to practice the claimed pharmaceutical composition with a reasonable expectation of success.

Substantiating evidence may be in the form of animal tests, which constitute recognized screening procedures with clear relevance to efficacy in humans. See Ex parte Krepelka, 231

USPQ 746 (Board of Patent Appeals and Interferences 1986) and cases cited therein. Ex parte Maas, 9 USPQ2d 1746.

Reasonable correlation must exist between the scope of the claims and scope of the enablement set forth. In view on the quantity of experimentation necessary the limited working examples, the nature of the invention, the state of the prior art, the unpredictability of the art and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

8. Claims 22-33 and 37-38 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of: a the fusion proteins of SEQ ID NO:4 and SEQ ID NO:35, pharmaceutical compositions and a kit thereof.

Applicant is not in possession of: **a recombinant Fel d 1 fusion product comprising a Fel d 1 chain 1, a Fel d 1 chain 2** and a linker selected from a carbon-nitrogen bond or a peptide linker consisting of 1 to 9 amino acid residues which links the N- terminal amino acid of one chain to the C-terminal amino acid of the other chain of claim 22; wherein the linker links the N-terminal amino acid of the chain 1 to the C-terminal amino acid of the chain 2 of claim 23; wherein **the chain 1 and the chain 2** are covalently bonded together by one or more disulfide bridges into an antiparallel arrangement of claim 28; wherein **the Fel d 1 chain 1 comprises a sequence of SEQ ID NO 1, or a homologue or fragment thereof** which provides substantially

the same allergenic properties as SEQ ID NO 1 of claim 29; wherein **the Fel d 1 chain 2 comprises a sequence of SEQ ID NO 2, SEQ ID NO 3, or a homologue or fragment thereof** which provides substantially the same allergenic properties as SEQ ID NO 2 or SEQ ID NO 3 of claim 30; wherein **the homologue has greater than 90% homology, preferably greater than 95% homology and particularly preferably greater than 99% homology** of claim 31; comprising **a sequence of SEQ ID NO 4** of claim 32; a homodimer consisting of two non-covalently associated **fusion products** as claimed in claim 22 of claim 33; a pharmaceutical composition comprising an immunotherapeutically effective amount of **the fusion product** as claimed in claim 22 and/or the homodimer as claimed in claim 33 and a pharmaceutically acceptable carrier, excipient or diluent of claim 37; and a **kit for the diagnosis of cat allergy comprising the fusion product** as claimed in claim 22 and/or the homodimer as claimed in claim 33 and instructions for use of the kit of claim 38 and as applied to claims 24-27.

Applicant has disclosed only the fusion proteins of SEQ ID NO:4 and SEQ ID NO:35, a pharmaceutical composition thereof and a kit thereof; therefore, the skilled artisan cannot envision all the contemplated fusion, pharmaceutical composition and kit possibilities recited in the instant claims. Consequently, conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method.

Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993). The Guidelines for the

Examination of Patent Application Under the 35 U.S.C.112, ¶1"Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 20001, see especially page 1106 3rd column).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 22-27 and 29-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vailes et al. (IDS filed on 03/22/2007) in view of George et al. (PTO-892 mailed on 11/16/2009; Reference U).

Vailes et al. teaches a recombinant Fel d 1 fusion product comprising a Fel d 1 chain 1 comprising SEQ ID NO:1 and a Fel d 1 chain 2 comprising SEQ ID NO:2 wherein the N-terminal amino acid of chain 2 is linked to the C-terminal amino acid of the chain 1 by way of a 19 amino acid linker which comprises a target site for NdeI and PstI enzymes capable of selective cleavage of the linker (In particular, Figure 1, 'Expression of Feld1 in baculovirus-infected insect cells' section on page 758, whole document).

Claims 22-27, 29-32 and 37 are included in this rejection because the recitation of a "carbon-nitrogen bond" linker in claims 1 and 24 is inherent in any amide bond.

Claim 32 is include in this rejection because the term "a sequence" of SEQ ID NO:4 reads on the instant fusion which comprises a subsequence of SEQ ID NO:4.

The claimed invention differs from the prior art in the recitation of "a peptide linker consisting of 1 to 9 amino acid residues" of claim 22; and "wherein the short peptide consists of 1 to 5 amino acid residues and preferably from 1 to 3 amino acid residues" of claim 25.

George et al. teaches that small linkers with 5 or less amino acids may be used to link chimeric proteins and that 5 amino acids linkers make the best linkers for gene fusion as they residues were most strongly preferred within natural linkers. The reference teaches that the linker length influences the desired function of the chimeric proteins and provides a scaffold to prevent unfavorable interactions between the two domains. The reference also teaches that the preferred linker amino acids are mostly hydrophilic, often polar and usually small. The majority, 59%, of the linker residues were in coil or bend structures with a mean length of 6.5 residues, but an average flexibility when compared to other protein regions (In particular, page 871, page 872, left column, last paragraph, whole document, Table II, paragraph spanning columns on page 875, Table VII). The reference also teaches in the abstract that choosing linkers is very important for obtaining desired function in chimeric multi-functional proteins. So, the teaching in George et al. is concerned with maintaining function of the individual components of the chimeric fusion protein.

It would have been obvious to one of ordinary skill in the art at the time of invention to substitute a 1 to 9 amino acid linker in the recombinant Fel d 1 fusion product comprising a Fel d 1 chain 1 and a Fel d 1 chain 2 wherein the N-terminal amino acid of chain 2 is linked to the C-terminal amino acid of the chain 1 by way of a 19 amino acid linker because George et al.

teaches that linker length may be optimized for function and the prevention of unfavorable interactions between the protein domains being linked. It would have been obvious to determine the optimal linker length to link the recombinant Fel d 1 fusion product of Vailes et al. and George et al. teaches that 5 amino acids linkers make the best linkers for gene fusion as they residues were most strongly preferred within natural linkers.

From the reference teachings, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the reference, especially in the absence of evidence to the contrary.

Applicant has submitted a 37 CFR 1.131 Declaration of Hans Gronlund and evidence in Exhibits A1 and A2 on 05/04/2010 to antedate the Vailes et al. reference.

Additionally, Applicant argues:

> For the record, Applicants also take issue with the examiner's assertion that the teachings of the George reference when combined with the teachings of the Vailes reference, are sufficient to render the present invention obvious, such that the claims of this application lack a special technical feature over the teachings of the references. Vailes et al. were seeking to engineer a recombinant Fel d 1 with antibody binding "comparable to that of the natural allergen." They further noted (second paragraph, second column of first page of the article) that "production of recombinant (r) Fel d 1 has been challenging .... " Vailes et al. then report on the preparation of a recombinant Fel d 1 having a 19 amino acid linker. One of skill in the art reading Vailes would come away with the clear understanding that a recombinant Fel d 1 is a challenging fusion product to prepare and that a lengthy linker is required to mimic the natural protein.
>
> Turning to the George reference, Applicants respectfully submit that the examiner misinterpreted Tables II - VII. These tables are not teaching the skilled person to use amino acid pairs as the linker; rather they are investigating the propensity of amino acid pairs within longer linkers. Page 875, first column, first sentence under the heading "Dipeptide propensities for linkers," explains that the authors are considering "dipeptide propensities for all linkers and medium sized linkers." The headings in Tables III and IV make it

clear that the authors are considering "all linkers" and "medium sized linkers," respectively - not dipeptides. Tables V and VI relate to "non-helical" and "helical" linkers, again suggesting longer linkers.

George et al. then provide a rather general conclusion in the final two columns. The reference certainly does not teach the use of shorter linkers. If anything, one of skill in the art would be taught that he should seek to investigate the structure of the 19 amino acid linker in Vailes et al. with a view to introducing more tailored diads. It also is important to note that George et al. are not concerned with specific problems concerning mimicking of the properties of naturally occurring Fel d I. George et al. therefore provide no more than suggestions for a lengthy research project into the nature of the linker in Vailes et al. The authors provide only suggestions for a lengthy research project into the nature of the linker used by Vailes et al. They certainly do not give one of skill in the art any expectation that one could reduce sensitization in a patient while simultaneously maintaining the immunological properties of the protein by providing a bond or a 1-9 amino acid linker.

This is not found persuasive because 37 CFR 1.131 affidavits or declarations are appropriate to antedate a reference or activity that qualifies as prior art under 35 U.S.C. 102(a) and not under 35 U.S.C. 102(b). 37 CFR 1.131 affidavits or declarations inappropriate where the reference publication date is more than 1 year prior to applicant's or patent owner's effective filing date. The one year grace period runs from the earliest US priority date, which is the filing date of PCT/IB04/01583 on 04/22/2004. Accordingly, the 37 CFR 1.131 Declaration of Hans Gronlund and evidence submitted on 05/04/2010 is ineffective to overcome the art.

Applicant's assertion that George et al. doesn't teach the use of shorter linkers is incorrect. Applicant's attention is drawn throughout the document and specifically to page 871 where the reference teaches that:

"The amino acids Thr, Ser, Pro and Asp were found to be desirable linker constituents. The author concluded that the preferred linker amino acids are mostly hydrophilic, often polar and usually small. The majority, 59%, of the linker residues were in coil or bend structures with a mean length of 6.5 residues, but an average flexibility when compared to other protein regions. It was suggested that pentapeptides consisting of Gly, Ser and

Thr would make the best linkers for gene fusion as they residues were most strongly preferred within natural linkers."

Further, Applicant's attention is drawn to page 872, left column, last paragraph where the terms 'small linker,' 'medium linker,' and large linker' are defined as being less than 6 amino acids, 6-14 amino acids and 14 or more amino acids, respectively. The reference also teaches in the abstract that choosing linkers is very important for obtaining desired function in chimeric multi-functional proteins. So, the teaching in George et al. is concerned with maintaining function of the individual components of the chimeric fusion protein and this teaching can be applied to the art of Vailes et al. to arrive at a Fel d 1/Fel d 2 fusion protein with a 1 to 9 amino acid linker.

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nora M. Rooney whose telephone number is (571) 272-9937. The examiner can normally be reached Monday through Friday from 8:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

June 15, 2010

Nora M. Rooney

Patent Examiner

Technology Center 1600

/Nora M Rooney/

Examiner, Art Unit 1644